Management of Otitis Media

An Interview

Jack Paradise & Tania Sih

. Jack, thank you for agreeing to discuss some important aspects of otitis media. What are the numbers that reflect the occurrence of this disease?

. In the United States, otitis media accounts for about 30 million office visits per year to physicians. It is the most common reason for illness office visits, it consumes about 3 to 4 billion dollars per year in cost, and the most common minor surgical procedure in the US is tympanostomy tube insertion, with over 300 thousand operations per year.

. The disease otitis media constitutes a spectrum of conditions. Could you comment on that?

. With acute otitis media (AOM), the tympanic membrane is bulging as pus under pressure fills the middle-ear cavity. As the illness subsides, the pressure diminishes and the liquid in the middle-ear cavity changes in character, becoming serous or mucoid and imparting an amber color to the tympanic membrane. This stage is most commonly referred to as otitis media with effusion (OME). Later, as healing progresses, air enters the middle-ear cavity and one sees an air-fluid level behind the eardrum. Finally, the fluid is resorbed or drains, and one sees a normal, translucent tympanic membrane. Transition from one of these stages of otitis media to another may occur in either direction. Perhaps most often, as noted above, the change is from AOM to OME. However, sometimes the illness begins with only OME, in association with upper respiratory tract infection, and then progresses to full-scale AOM. Things can get better or they can get worse.

. Let us divide this discussion into two parts, AOM first, and then OME, recognizing that there is no clear line of demarcation between the two conditions. However, for conceptual purposes, it's much easier to discuss them separately.

. OK! So first, AOM. The bacteriology is familiar, I'm sure, to most readers. *Streptococcus pneumoniae* accounts for the largest share of the etiologies of acute otitis in most parts of the world, averaging about 30 percent of cases. Close behind, in second place, is *Haemophilus influenzae*, usually beta-lactamase positive, accounting for about 25 percent of cases. *Moraxella catarrhalis* accounts for about 12 percent of cases. Group A beta-hemolytic *Streptococcus pyogenes* (GAS) accounts for only a very small percentage, perhaps 2 percent, whereas in earlier years it accounted for a much larger share. Finally, in most reported series of children with AOM, no bacterial growth can be recovered in about 30 percent of the cases.

. Should we routinely treat all episodes of AOM with an antibiotic?

. The arguments in favor are as follows: **First**, usually there are pathogenic bacteria present. **Second**, there is good evidence that one obtains a more rapid and more certain outcome than with no treatment at all. **Third** is the secular decline in suppurative complications such as mastoiditis, epidural abscess, and brain abscess. Those conditions used to be quite common in the early part of the twentieth century, and their decline has paralleled the increased use in antibiotics. It seems quite reasonable to imagine that antibiotic use has been responsible, at least in part, for that decline in complications. **Finally**, mastoiditis rates are reportedly higher in the Netherlands, where antibiotic use is often withheld, than in other European countries and the United States - although even in the Netherlands, apparently, the rate is low, so it's clear that the risk of mastoiditis from withholding antibiotic is not great.

. The main argument against routinely treating all episodes involves the fact that bacterial resistance is very much stimulated by antibiotic use.

. And besides, one also deals with the adverse side effects of antibiotics, and finally, the cost. The principal problem that we have worried about in the past 10 or so years has been the increasing emergence of multiply resistant *Streptococcus pneumoniae*. The contributing factors to that phenomenon are previous treatment with antimicrobial drugs, particularly with beta-lactams; daycare attendance or heavy exposure to numbers of other children at home - the critical factor here is the number of children, not the location of the exposure; and finally, age less than two years.

. Over the years, there has been a very steady increase in resistance in general and a specific increase in strains that are fully resistant.

. In our own hospital in Pittsburgh, during the period from 1991 to 1995 there were practically no resistant isolates of *S. pneumoniae*. Since then the proportion of isolates that are penicillin-resistant has increased progressively, so that by 2003 nearly 60 percent of the middle-ear isolates from young children were penicillin-resistant.

. How about macrolide resistance?

. With respect to the macrolide resistance of *S. pneumoniae*, there has been a similar gradual, and then more abrupt, increase over the period from 1992 to 1999, at which time over 30% of the *S. pneumoniae* isolates were resistant to macrolide. And with respect to ampicillin resistance, we have seen over the past decade an increasing proportion of *Haemophilus influenzae* isolates that are resistant to ampicillin by virtue of the fact that they are producing beta-lactamase.

. In Latin America, specifically in Argentina, Brazil, and Mexico during the period 1999 to 2000, the following values have been reported: resistance on the part of *S. pneumoniae* isolates to penicillin was 42 percent, with 15 percent of the isolates fully resistant; 15 percent were erythromycin-resistant. Of the isolates of *H. influenzae* - only 17 percent produced beta-lactamase, a value lower than in the United States, where the values are now in the 30-40 percent range. And, as in the US, 99 percent of the isolates of *Moraxella catarrhalis* produced beta-lactamase, and accordingly were amoxicillin-resistant.

. For that reason microbiological surveillance is important.

. Recently in the US, the American Academy of Pediatrics and the American Academy of Family Physicians issued a clinical practice guideline with respect to the use of antibiotics in treating children with AOM. Could you comment on that?

. For the first time, that guideline offered what was called an observation option. That is, the option, not the necessity, to defer antibacterial treatment for 48 to 72 hours, and instead to offer only symptomatic relief. The guideline indicated that the observation option would be appropriate only when satisfactory follow-up of the children could be assured, and when it was clear that antibacterial treatment could be started if symptoms persisted or worsened.

. The guideline also provided specifics as to when antibacterial treatment should be used and when it might be withheld at the physician's discretion. Could you comment on those?

. In children under six months of age, when the diagnosis of AOM is certain, the guideline recommended antibiotic treatment. Also, if the diagnosis is uncertain - and the guideline recognizes that it is sometimes impossible to make a certain diagnosis (although I think they were too lenient in that regard) - the guideline recommended antibacterial treatment.

. How about for children six months to two years of age?

. In the six months to two years age group, the guideline again recommended antibacterial treatment if the diagnosis of AOM is certain, and antibiotic treatment also if the diagnosis is uncertain, but the illness is "severe." The observation option was available if the illness is "non-severe." "Non-severe" was defined as mild pain and a temperature of less than 39ºC in the preceding 24 hours.

. And for children two years of age and older?

. In children two years of age and older, the guideline recommended antibacterial treatment when the diagnosis is certain and the illness is severe, but the observation option if the illness is non-severe. And if the diagnosis is uncertain, again the observation option is available at the physician's discretion.

. Do you agree with this guideline?

. I have some concerns about the guideline. **First** of all, the studies that the guideline was based on were themselves flawed or limited. Specifically, the diagnostic criteria for AOM were not very stringent, so that many of the subjects studied may have had OME or no ear disease at all. In addition, in none of those supporting studies was early symptomatic response measured or documented. That is to say, within the first 24 or 48 hours, when discomfort is usually at its maximum, almost none of the studies provided information as to how children were responding symptomatically during that early period, and focused only on later points in the children's course.

Secondly, there are certain studies have found that withholding antibiotics gave less favorable results than treating with antibiotics, and the results of those studies have been misinterpreted or underestimated, or both.

And **thirdly**, the guideline actually sanctions antibacterial treatment of infants who don't have a diagnosis, which I am troubled by, because treating children

with antibiotics who do not have a clear diagnosis may, on the one hand, lead to inappropriate treatment of viral illness, which shouldn't be treated at all, or on the other hand, to inadequate treatment of severe illness which should be treated more vigorously.

. Your own opinion?

. My own opinion is that one should certainly treat all children who have definite AOM *and* 1) are less than 5 years of age; or 2) are ill systemically; or 3) appear to have severe infection; or 4) have recent histories of recurrent AOM; or 5) may not get satisfactory follow-up. However, for children five years of age or older who have definite but mild AOM, the observation option seems reasonable.

. If you choose to treat, which antimicrobial would you consider?

. If one is going to treat, I think there is a consensus that **amoxicillin** should be used as first-line treatment, for a number of reasons: **First**, amoxicillin is the most effective orally-administered antibiotic against multiply-resistant *S. pneumoniae*, especially if it is used at higher dosage, as I will mention later. **Second**, some of the cases caused by beta-lactamase-producing organisms will nonetheless resolve with amoxicillin treatment. **Third**, amoxicillin is extremely safe. **Fourth**, amoxicillin is palatable; children will take it. **Fifth**, it can be given twice daily rather than three times daily. And **finally**, it is relatively inexpensive.

. What about dosage of the drug?

. In view of the increasing prevalence of resistant *S. pneumoniae*, dosage in young children should be increased to 80-90 mg or even 100 mg/Kg/day. On the other hand, children who are over two years of age, who have had no recent antibiotic exposure, and who are not attending daycare can receive the more traditional dosage at half that level, or 40 to 45 mg/Kg/day.

. And when the child does not respond to amoxicillin?

. For the child with AOM who fails to respond satisfactorily to amoxicillin, clearly the drug of choice is amoxicillin-clavulanate, provided that the child is not allergic to penicillin and is able to tolerate the drug - the main side-effect being diarrhea. Newer formulations of the drug, however, are associated with a relatively low incidence of severe diarrhea.

. When amoxicillina and amoxicillin-clavulanate cannot be used?

. If amoxicillin-clavulanate cannot be used, then the choices are cefdinir, cefuroxime axetil, azithromycin, and intramuscular ceftriaxone. Cefdinir and cefuroxime may be somewhat less effective than amoxicillin, and cefuroxime tastes so unpleasant that children almost uniformly refuse to take it. Azithromycin is palatable but less broadly effective than the other orally administered drugs. Intramuscular ceftriaxone is very effective but has its own adverse features. Among these are the pain of injection, the higher cost of the drug in comparison with that of other agents, and the fact that multiple doses may be necessary in severe or persistent cases, and in any case are more effective than a single dose. I believe that intramuscular ceftriaxone has its place in the armamentarium, but it is appropriate only in very selected cases.

. How long should we treat children who have AOM with an antibiotic?

. The best designed clinical studies, together with clinical experience, suggest that

courses of **antibiotic treatment that are shorter than 10 days should not be used in children less than two years of age**. **Shorter courses may be sufficient for children who are older and who have mild illness**. In some instances, courses longer than 10 days will be necessary, particularly for infants and even for some older children with persistent or severe disease. The physician should **individualize the duration of treatment**, taking all of the clinical factors into account, and not automatically use the same duration for every child.

. How can we prevent recurrent AOM?

. A number of measures are available. The most important measure, if we were able to accomplish it, would be to reduce poverty and improve living conditions, because more than anything else, the most influential environmental factor in promoting the occurrence of otitis media is poverty.

- **Breast feeding** provides some measure of protection but the degree of protection is limited.
- It might be helpful to **avoid exposure to cigarette smoke**, although that presumed association may be confounded by socioeconomic status.
- **Reducing exposure to large numbers of other children (day care)**, when that is possible, would be helpful, because clearly, exposure is an important factor.
- The use of heptavalent (seven-valent) **pneumococcal conjugate vaccin**e has an important place, although its effectiveness in preventing otitis media specifically is limited.
- **Influenza vaccine** perhaps provides a measure of protection indirectly, by reducing the occurrence of influenza.
- **Antimicrobial prophylaxis has some value, but risks encouraging the emergence of resistant organisms**.
- When recurrences exceed the threshold of parental tolerance, a resort to surgery with the **insertion of tympanostomy tubes (TT)** is usually quite effective for as long as the tubes remain in place.
- For children in whom recurrences continue after TT have been extruded, **adenoidectomy** has substantial although also limited efficacy.
- Finally the use of **xylitol chewing gum or syrup** may be somewhat protective, although the supporting studies are not strong, and the practicality of its usage is dubious because of the frequency with which it has to be administered throughout the day.

. Let us to move on to otitis media with effusion (OME).

. In this condition the middle-ear cavity contains usually sterile liquid of variable viscosity. The available information about the natural history of OME is somewhat limited. One study of infants with AOM, together with the **progression of their AOM to OME**, and the subsequent course of their OME, is illustrative of the information we have. In that study, at the beginning of the period of observation, 100 percent of the affected ears contained effusion, which of course at that time was by definition purulent. **By one month** into the illness, the proportion of **ears showing effusion was down to about 50 percent**. **By two months** the proportion was down to about **25 percent**, and **by three months**, down to about **20 percent**. Beyond three months after the onset of AOM or OME, we have very limited

information concerning the course of children who continue to have effusion. The reason, I believe, is that when children remain under close observation, some intervention - namely tube insertion - has usually been undertaken after about three months of effusion. Alternatively, in the situations where no intervention has been undertaken, there hasn't been careful documentation and reporting of the progression from that time forward. So **we really don't know what proportion of children by, say, 12 months or 24 months after onset, have cleared their effusions spontaneously, without treatment**.

. What about the management of OME?

. Although **antihistamines and decongestants** have been used for many years, they are not effective and **should no longer be used**, particularly because of their adverse side-effects. Antimicrobials do have limited efficacy in treating OME, but there is the risk of encouraging the emergence of resistant *S. pneumoniae* from their continuous use. **Steroids have a degree of short-term benefit** in treating OME, but **only short-term**, and one faces the risk that a child receiving steroids who develops varicella might proceed to having a more devastating course. So, in summary, **I think that steroids have no practical use in treating OME**.

. Mucolytic agents?

. Mucolytic agents have been advocated for the treatment of OME but are probably **not effective**. Allergic management of children may be helpful in those particular children who have allergic rhinitis, but certainly **allergic management has nothing to offer in children who are not otherwise allergic**.

. Surgery?

. Insertion of TT is clearly effective in treating OME, but it carries the risk of certain complications, as discussed later. And finally, adenoidectomy has limited efficacy, but one would want first to try TT insertion as a less drastic form of intervention. Then, in the child who persists in developing effusions after the tubes have been extruded, adenoidectomy offers some additional chance of relief.

. Historically, over the years, people have been concerned about persistent OME because of its possible complications and sequelae. Could you discuss these?

. **First** of all, there is the heightened risk of developing AOM, although it is not clear whether that risk is because of the effusion itself or because the child is otitis-prone. Nonetheless, we know from experience the children with persistent OME are often likely to progress to episodes of AOM. **Second**, if OME persists over long periods of time, there has been concern that structural middle-ear changes can occur, for example, atelectasis or cholesteatoma. **Third**, there has been some evidence that persistent OME, even without any acute infection, can result in damage to the cochlea with resulting sensorineural hearing loss - although I believe the evidence for that is not very strong. And **finally**, there has been concern about various types of developmental impairment that children might incur because of the fact that persistent OME is usually accompanied by some degree of conductive hearing loss, and the hearing loss, in turn, has been considered to be a type of sensory deprivation that can interfere with various aspects of children's development, particularly speech, language, cognition, and psychosocial development.

. You have written as follows: "The supposition has been that because children are not receiving entirely accurate auditory input during their formative first two or three years of life, the various cortical relationships that have to be formed that depend on hearing, are never formed correctly, and the child is left with what one might consider to be a developmental scar, such that even after the otitis resolves and the hearing returns to normal, there remain deficits in the child's abilities in the areas of speech, language, learning, and psychosocial development." Could you be more specific about the aspects of development researchers have been concerned about?

. If one considers the very young child's developmental tasks, they are quite simple and can be summarized in a few words: to listen, to learn, to understand, to think, to speak, and to get along with other children. Moving along to the school- age child's developmental tasks: to be able to listen in noisy environments, to pay attention, to concentrate, to integrate, to read, to write, to cope with stress, and to interrelate with other children. Every one of these developmental abilities has been considered by some investigators to have been damaged, or hampered, or interfered with, by children having had persistent OME early in life, during their formative years of development.

. Could you cite examples of the kinds of studies reported?

. Examples of the titles of reports in professional journals that have reflected concerns about this issue include the following:

- "otitis media in infancy and intellectual abilities, school achievement, speech, and language at age 7 years";
- "effects of recurrent otitis media on language, speech and educational achievement";
- "early otitis media and later educational risk";
- "recurrent otitis media and parenting stress in mothers of two-year-old children";
- "recurrent otitis media during infancy and linguistic skills at the age of nine years" .

These are some selected titles from perhaps 50 or more reports in the literature expressing concern about the fact that unless something is done about OME, after a short period, children will as a result be damaged in a way that persists throughout their later years. Reports such as these extending over the past three decades have served to warn practitioners and parents alike that if a child has persistent OME, he or she might grow up to be less intelligent than otherwise, or less articulate, or less accomplished, or less attentive, or less capable, or less well-adjusted psychologically.

. In keeping with those concerns, various official agencies have issued guidelines recommending the treatment of persistent OME. In 1994, the United States Agency for Health Care Policy and Research, now known as the Agency for Health Care Research Quality, issued a guideline that was meant to apply to **children 1 to 3 years of age**. Could you describe that guideline?

. For children in that age group **who have middle-ear effusion for three months**, and in addition, have **bilateral hearing loss defined as 20 decibels or greater**, the

guideline recommended **antibiotic treatment or tympanostomy (i.e. ventilating) tubes**. For children with **effusion for 4 to 6 months and bilateral hearing loss**, the guideline simply recommended **tympanostomy-tube** insertion.

More recently, in the year 2000, the American Academy of Otolaryngology Head & Neck Surgery issued guidelines for **children** in general – **no specified age**, but presumably mainly younger children - and that guideline simply recommended that **if effusion has persisted for more than three months**, without mention of hearing levels, **tubes should be inserted**.

. As you have written, there are, however, many problems regarding the studies purporting to show a relationship between children's development and their earlier-life OME. Could you comment on those problems?

. I have spent many years thinking about those studies. **First,** one must be impressed with the fact that the studies have had many methodological limitations. **Second,** the results have not been consistent. And **finally**, all of the studies have been associational in nature. That is to say, they found that children who had more otitis media early in life had poorer development when they grew older. Or, on the other hand, they examined the relationship between development later in life and early-life otitis media, and found that some children who had limitations in learning or in speech or language had had histories of considerable otitis media in the past. However, we all know that association is not equivalent to causality. None of the studies that have been reported specifically addressed the issue of whether persistent OME earlier in life actually **caused** later developmental impairment. And none of the studies, even those recommending intervention, examined the possible effects of intervention, intervention being, of course, TT insertion.

Thus, even if one does find an **association** between early life OME and later developmental impairment, the question remains whether the persistent OME actually **caused** the lasting developmental impairment. One can think of a number of confounding factors that might predispose children to having both early life OME and later-life developmental impairment. Such factors might be genetic in nature, or involve perinatal difficulties, socioeconomic problems, or various kinds of environmental circumstances. Any such factors, you can well imagine, might readily predispose children on the one hand to having a lot of otitis media early in life, and on the other hand to have somewhat less favorable developmental outcomes than their peers.

. Issues of causality aside, a further critical question is whether TT insertion can prevent or lessen long-term developmental impairment. How would one approach that question?

. I came to believe that what was needed in order to address this issue of causality was, first, to assemble a large group of infants and young children, all of whom had well-documented persistent middle ear-effusion. Then one would randomly assign them to receive or not receive an intervention that would largely result in clearance of the effusion, namely, insertion of TT. Thereafter, the two groups would be compared prospectively regarding their long-term developmental outcomes. By instituting a clinical trial such as this, one would hope that, in one

group, the tubes would have largely cleared the effusion, whereas in the other group, not having received tubes would have allowed the effusion to continue. Thus, one would have created, from a homogeneous group of children, one group of children whose ears from that point were mainly clear and whose hearing was mainly normal, and an otherwise similar group, many if not most of whom continued to have the disease.

. Tell me about the study you instituted in Pittsburgh.

. In 1991, over a period of four years we enrolled 6,350 healthy infants less than two months of age at two hospital clinics and six private pediatric group practices in the greater Pittsburgh area. We monitored their middle-ear status monthly in order to identify children who developed, within the first three years of life, continuous bilateral middle-ear effusion for 90 days, or continuous unilateral middle-ear effusion for 135 days, or intermittent bilateral or intermittent unilateral effusion for specified proportions of longer periods. Once we identified those children, we randomly assigned them either to the early-tube group who received tube insertion as soon as we could arrange it or to a later tube group where the children would receive tubes only after six months if bilateral effusion persisted or after nine months if unilateral effusion persisted. However, if their effusion cleared spontaneously within those time periods, they didn't receive tubes.

Over a period of more than four years, we enrolled over 6,000 infants. Of those, we were able to identify and randomly assign 429 with sufficiently persistent OME to be eligible for our clinical trial. Of those 429, 216 were assigned to the early-tube group and 213, to the delayed-tube group. In both groups of children, we then conducted a series of developmental tests when the children reached age three, age four, age six, and ages nine to 11 years.

What was our degree of success in creating two groups of children who differed only with respect to their percent of time with effusion after being randomized? In the early-tube group, 21% of the children had middle-ear effusion at least 50% of the time during the six months after randomization, compared with 64% of the children in the delayed-tube group. The values were similar during the following six months. Thus we didn't accomplish an all-or-none separation, but we were able to separate the children into one group that had relatively little middle ear-effusion after randomization, and another group who had quite a lot of middle-ear effusion after randomization.

At the various follow-up ages we used a number of tests to assess the children's development. First, a group of formal, norm-referenced tests of cognition, receptive language, and phonological memory. Next, all of the children had tape-recorded conversational speech samples obtained, and from those samples we tested very accurately their expressive language skills and their speech sound production skills, that is, their articulation of words. At ages nine to 11 years, we tested the children for literacy skills, phonological awareness, auditory processing skills, attention, intelligence, and academic achievement. And finally, we used parent-report inventories to assess parent-child stress and the children's behavior.

. Which were your test results in children at the age of three years?

. Our test results in the children at the age of three years showed no statistically

significant differences favoring the early-tube group over the delayed-tube group on any measure of cognition, language, speech, or psychosocial development. Again at age four, there were no statistically significant differences favoring the early-tube group over the delayed tube-group. And again at age six years there also were no statistically significant differences favoring the early-tube group over the delayed-tube group on any measure of development.

. Was there some correlation with children's socioeconomic status?

. Yes, by contrast, the results on most measures at each age were very strongly related to children's socioeconomic status. Consistently, the results were most favorable among the most advantaged children and least favorable among the least advantaged children, and those differences were very large.

. Your conclusion?

. In conclusion from that study, we would say that in children with persistent middle-ear effusion in the first three years of life, within the durations that we used in the study - because we were not willing to let children continue indefinitely with middle-ear effusion - early tympanostomy-tube insertion did not have a beneficial impact on any developmental outcome at ages three, four, and sixyears of age. A conclusion that follows logically is that great restraint is necessary when considering tympanostomy-tube insertion for young children with otherwise uncomplicated persistent middle-ear effusion.

. Jack, you have indicated that there are some caveats concerning these results that are important to mention.

. Yes, **first**, one cannot generalize the results to children with certain handicapping conditions, for example Down syndrome, or to children with other major health problems. **Second**, one cannot generalize the results to children with periods of effusion longer than those we studied, because longer periods might have adverse consequences. And **finally**, children whose effusion is consistently accompanied by hearing loss that is more severe than the usual mild to moderate degree of loss also should not be included among those for whom these conclusions are relevant.

Not yet available are our final test results in our children at ages nine to 11 years. We are just completing those tests. We have tested the children for literacy skills, phonological awareness, auditory processing skills, attention, psychosocial function, intelligence, and academic achievement. Each of those attributes has been considered by some investigators to be placed at risk by early-life otitis media, and our study won't be completed until we assess all of these results.

. So, given what we know now, which children should actually receive tubes?

. Before facing that question one needs to examine the various complications and sequelae of tubes. These include premature extrusion of the tubes; obstruction of the tube lumen; tube otorrhea, which is common after receiving tubes; dislocation of the tube into the middle-ear cavity; and the need to protect the children's ears from water - although that is somewhat controversial, we continue to feel that there is a risk to children who swim without protection. Structural sequelae include tympanic membrane perforations, tympanosclerosis, atrophic scars that can predispose to atelectasis or retraction pockets, and cholesteatoma. Finally, there is

concern about possible later hearing loss, although that remains to be clarified.

. So in summary, what would you recommend?

. My own opinion is that otitis media with effusion persisting for up to one year in children less than three years of age is probably harmless in the long run, provided that there are no associated symptoms, and provided that, with periodic observation, no pathologic changes in the eardrum become apparent. Effusion persisting for even longer periods may also be harmless, but I don't think we have enough information to make that assumption. Once a child's effusion has persisted to the point where one is considering tube insertion, a course of second-line antibiotic treatment may sometimes prove effective in clearing the effusion, thus avoiding the need for surgery. Certainly antimicrobial treatment is appropriate at that point if there is purulent nasal discharge, because so long as nasopharyngeal or sinus infection continues, one can be confident that the middle-ear effusion will persist. If effusion persists after a course of antimicrobial treatment and after the nasal discharge has subsided, the decision whether to proceed with tube insertion is best individualized, based on a number of parent-related and disease-related variables. Variables that would operate in favor of inserting tubes would include sustained hearing loss if the degree of loss is moderately severe or severe; significant problems with a child's speech or language development; the occurrence, in addition to OME, of frequent episodes of AOM; the occurrence, in children who develop AOM, of adverse reactions to a range of antimicrobial drugs; and finally, in the child with recurrent AOM, regular exposure to large numbers of other children, because such exposure heightens the risk of the child's becoming colonized with resistant organisms, an outcome rendered even more likely by superimposition of additional antimicrobial treatment.

Variables that would argue against the insertion of tubes would be the following: normal or near normal auditory acuity; age-appropriate speech and language skills; a recent history relatively free of AOM; soon-to-be-expected warm weather (during the summer OME usually clears spontaneously); effusion limited to one ear; and finally, because we as physicians often don't know with certainty the correct course to follow, parental reluctance concerning surgical intervention.

. Jack, do you still have time for more questions?

. That's up to you, Tania.

One question regards the indication for macrolide treatment for a child with AOM. I would like to ask you when you would recommend a macrolide such as azithromycin for a child with AOM.

. It would not be my first choice of drug, but if a child is allergic to all beta-lactam drugs, that is, the penicillins and cephalosporins, then I think azithromycin would be a reasonable choice. Not optimal because its spectrum is more limited than that of other drugs, but one's choices are also limited. Another circumstance might involve the child to who is very difficult to medicate, because he or she spits out everything that anybody adminsters. Azithromycin tastes pretty good, so if one is unable to get any other drug in, sometimes the child will take azithromycin. The same is true, however, of cefdinir; the preparation available to us is also quite palatable. So those would be the two drugs for the child who is extremely resistant

to taking medication. However, I believe that the preferred first-line drug would be amoxicillin and the preferred second-line drug, amoxicillin-clavulanate.

. Thank you, Jack. So, in summary, macrolides could be used: a) in children that are allergic to beta-lactam drugs and b) in children that are difficult to medicate. But really, they are not a good choice, because their spectrum is more limited than that of other drugs. Also, the drug does not have good middle ear penetration and increasing macrolide resistance is a major concern.

I have another question for you Jack, besides macrolides. We live in a part of the world, here in Brazil for instance, in which *Streptococcus pneumoniae* resistance levels to penicillin is very low. For instance, we have intermediate resistance levels to penicillin of about 10%, and high levels of resistance only 2-3% in some cases. So, in a place where you have low levels of *Streptococcus pneumoniae* resistance, would you even consider giving the higher dosage of amoxicillin to those children? It's in a geographic variation completely different from yours, you live in US, where in some places you have over 60% of high-level of penicillin resistance to *Streptococcus pneumoniae*. What's your opinion, what do you do in these cases?

. That's a fair question, I think, and I think one can vary practice based on information you have available. I'd first ask you, are those levels of resistance taken from middle-ear isolates or are they from patients with sepsis or adult patients with pneumonia, or similarly invasive infection? What type of patient provides the sort of data that you've just cited? Because if they're not middle-ear isolates, the reported level of resistance might be considerably lower than is actually the case in isolates from the nasopharynx or the middle ear.

. This was the result of a huge national project of surveillance that it was done over the years with over four thousand samples, but from invasive diseases. So we don't know exactly…

. Right, those data may not reflect the situation in the middle ear. The question is what are the **reasons not to give high doses of amoxicillin**? In the US, at least, it's a very inexpensive drug; it's non-toxic; there's a huge margin of safety; and **higher doses are more effective than lower doses against resistant** . So the way I think about it, if a child is willing to take the higher dose, I see very little reason not to give it. On the other hand, it may well be the case that it is not necessary to give the larger dose, and if cost is a factor, or the child is resisting being given any medication, then the chances are probably pretty good that the more standard doses, that is, lower doses, would be effective. **Again, one could individualize based on a child's past history**. **If a child has had a lot of trouble in the past** and you want to be certain that you are getting the most benefit possible, **you might use a larger dose**. On the other hand, if **it's a first episode or a second and the child hadn't been ill very much**, he or she might very well be **OK with a smaller dose**.

. Ok Jack, I'm not talking about an under two year-old child that had recurrent bouts of infection, of AOM, and is in daycare. I'm talking about the type of child one encounters more routinely, so this answer of yours was very important.

I have another question about the use of ceftriaxone, which you might need,

for example, in children with compliance problem or gastrointestinal problems. Should we use one or three doses, one or three shots?

. There is good evidence to show that in severe illnesses three doses are more effective than one dose. But ordinarily one would not use ceftriaxone for mild illness, so that for the most part when you're using it, you are using it because you're concerned about the child's outcome, and under those circumstances I would give one injection every third day for a total of three injections.

I have another question about otorrhea, when you put ear tubes, that's sometimes is a frequent complication. What's your opinion about that?

. Well, it certainly is a frequent complication, and it's one of the reasons, I think, to be reluctant about, or conservative about putting ear tubes in. My best understanding is that currently ofloxacin is probably the topical medication of choice to use. Infrequently it becomes necessary to treat children with systemic antibiotic, but usually I think topical ear drops with ofloxacin or ciprofloxacin should be satisfactory. It's a nuisance for most part, rather than a serious problem.

. So the ofloxacin otic drops would be very efficient in this case.

. Yes, indeed.

. OK, thank you so much Jack, I really appreciate your effort!

. It was a pleasure for me. Thank you very much for your attention.

Recommended readings

1. Dowell SF, Butler JC, Giebink GS, et al. Acute otitis media: management and surveillance in an era of pneumococcal resistance--a report from the Drug-resistant Streptococcus pneumoniae Therapeutic Working Group. Pediatr Infect Dis J 1999;18:1-9.
2. Paradise JL, Bluestone CD, Colborn DK, et al. Adenoidectomy and adenotonsillectomy for recurrent acute otitis media: parallel randomized clinical trials in children not previously treated with tympanostomy tubes. JAMA 1999; 282:945-53.
3. American Academy of Pediatrics Subcommittee on Management of Acute Otitis Media. Diagnosis and management of acute otitis media. Pediatrics 2004;113:1451-65.
4. Paradise JL, Feldman HM, Campbell TF, et al Tympanostomy tubes and developmental outcomes at 9 to 11 years of age. N Engl J Med 2007;356:248-261.